

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Currently Amended) A method of inhibiting the lethal effect of expressing an otherwise lethal protein in a cell, said method comprising the steps of:

(a) providing a cell, tissue or organism having (i) a nucleotide sequence encoding a Gas1 protein, ~~or a functional equivalent, derivative or bioprecursor thereof~~, which is capable of inducing apoptosis in said cell and (ii) a further nucleotide sequence encoding a protein which is otherwise lethal to said cell in itself or in response to a lethal stimulus in the presence of Gas1

wherein said otherwise lethal protein is selected from the group consisting of metabotropic glutamate receptors, ionotropic glutamate receptors, excitatory amino acid receptors, cytokine receptors, chemokine receptors, monoamine receptors, peptide receptors, kinases, and caspases;

(b) inhibiting function and/or expression of said Gas1 protein ~~or functional equivalent, derivative or bioprecursor thereof~~; and

(c) expressing said further sequence encoding said otherwise lethal protein wherein said otherwise lethal protein normally induces ~~the expression or activate either the Gas1 protein or a protein in the signal transduction pathway of which Gas1 is a component~~ Gas1-mediated cell death.

2. (Withdrawn) A method of identifying compounds which inhibit or enhance expression or activity of proteins which are lethal to a cell, tissue or organism said method comprising the steps of:

(a) providing a cell, tissue or organism comprising a nucleotide sequence encoding a Gas1 protein or a functional equivalent, derivative or bioprecursor thereof, which is capable of inducing apoptosis in said cell, and ii) a further sequence encoding a protein which is otherwise lethal to said cell in itself or in response to a lethal stimulus in the presence of Gas1;

(b) inhibiting function and/or expression of said Gas1 protein or functional equivalent, derivative or bioprecursor thereof or a protein in the apoptotic pathway of which Gas1 is a component;

(c) expressing said sequence encoding said otherwise lethal protein;

(d) contacting said cell with a compound to be tested; and

monitoring the effect of said compound on said otherwise lethal protein compared to an identical cell which has not been contacted with said compound

wherein said proteins normally induce the expression or activate either the Gas1 protein or a protein in the signal transduction pathway of which Gas1 is a component.

3. (Withdrawn) A method according to claim 2 wherein said expression or activity of Gas1 protein is inhibited by providing a nucleic acid molecule in said cell which is capable of hybridising to mRNA corresponding to Gas1 DNA to prevent expression thereof.

4. (Withdrawn) A method according to claim 2 wherein said expression or activity of said Gas1 protein is inhibited by inhibiting the expression or activity of a protein in the pathway of which Gas1 is a component.

5. (Withdrawn) A method according to claim 2 wherein said cell is induced to express said Gas1 protein by contacting said cell with a stimulus that increases intracellular calcium levels in said cell.

7. (Withdrawn) A method according to claim 2 wherein said further sequence encoding said otherwise lethal protein is expressed by providing it on a suitable expression vector.

8. (Withdrawn) A method according to claim 2 wherein said lethal protein is a highly expressed recombinant protein.

9. (Withdrawn) A method according to claim 2 wherein said otherwise lethal protein comprises any of a glutamate, NMDA, AMPA or kainate receptor.

10. (Withdrawn) A method according to claim 9 wherein said glutamate receptors comprises any of a type 1 to 8 metabotropic receptor.
11. (Withdrawn) A method according to claim 3 wherein said nucleic acid molecule is provided as an oligonucleotide or as a vector including a nucleotide sequence of said nucleic acid molecule.
12. (Withdrawn) A method according to claim 11 wherein said nucleic acid molecule comprises an oligonucleotide consisting of the nucleotide sequence depicted in Sequence ID No. 5.
13. (Withdrawn) A method according to claim 11 wherein said nucleic acid molecule further comprises ribozyme or DNAzyme activity.
14. (Withdrawn) A method according to claim 2 wherein said Gas1 protein is of mammalian origin.
15. (Withdrawn) A method according to claim 14 wherein said Gas1 protein is from any of a human, mouse or rat.
16. (Withdrawn) A method according to claim 14 wherein said Gas1 protein comprises the amino acid sequence depicted in either of Sequence ID No. 2 or 4 or a functional equivalent, derivative or bioprecursor thereof.
17. (Withdrawn) A compound identifiable as an inhibitor or an enhancer of expression or activity of an otherwise lethal protein according to the method of claim 2.
18. (Withdrawn) A pharmaceutical composition comprising a compound according to claim 17 together with a pharmaceutically acceptable carrier, diluent or excipient therefor.
- 19-21. (Canceled).

22. (Withdrawn) The method of claim 54 wherein said cell is associated with a disease condition selected from the group consisting of a neurological disorder, a cardiovascular disorder, an autoimmune disorder, a neuroendocrine disorder or cancer.

23. (Withdrawn) A method of monitoring the severity of a disease condition mediated by cellular apoptosis in a cell, tissue or organism comprising measuring the level of expression or activity of a Gas1 protein or a functional equivalent, derivative or bioprecursor thereof in said cell or tissue or organism.

24. (Withdrawn) A nucleic acid molecule encoding a rat Gas1 protein or a functional equivalent, derivative or bioprecursor thereof, comprising an amino acid sequence according to Sequence ID No. 2.

25. (Withdrawn) A nucleic acid molecule encoding a protein capable of inducing apoptosis in a cell comprising an amino acid sequence according to Sequence ID No. 4 or a nucleic acid molecule complementary thereto.

26. (Withdrawn) A nucleic acid molecule according to claim 25 which is a DNA sequence.

27. (Withdrawn) A nucleic acid molecule according to claim 26 which is a cDNA molecule.

28. (Withdrawn) A nucleic acid molecule according to claim 26 comprising the sequence of nucleotides according to Sequence ID No. 1.

29. (Withdrawn) An antisense molecule capable of hybridising to the nucleic acid molecule of claim 25 under conditions of high stringency.

30. (Withdrawn) An antisense molecule according to claim 29 comprising a sequence of nucleotides according to Sequence ID No. 3 or 5.
31. (Withdrawn) A protein encoded by the nucleic acid molecule of Sequence ID NO. 1 or a nucleic acid molecule capable of hybridizing to Sequence ID NO.1 or its complement under conditions of high stringency.
32. (Withdrawn) A protein comprising the amino acid sequence illustrated in Sequence ID No. 2.
33. (Withdrawn) A protein capable of inducing apoptosis in a cell comprising an amino acid sequence according to Sequence ID No. 4 or a functional equivalent, derivative or bioprecursor thereof.
34. (Withdrawn) An expression vector comprising a nucleic acid molecule according to claim 25 or a nucleic acid molecule capable of hybridizing to Sequence ID No.1 under conditions of high stringency.
35. (Withdrawn) An expression vector according to claim 34 wherein said vector is any of a plasmid, virus or phage derived vector.
36. (Withdrawn) An expression vector according to claim 34 comprising a tissue or cell specific promoter.
37. (Withdrawn) An expression vector according to claim 34 further comprising a sequence encoding a proapoptotic protein.
38. (Withdrawn) An expression vector according to claim 34 which is inducible for expression of a protein comprising the amino acid sequence of Sequence ID No.2 or a polypeptide capable of inducing apoptosis in a cell.

39. (Withdrawn) An expression vector according to claim 38 comprising the inducible vector pIND.
40. (Withdrawn) A host cell, tissue or organism, transformed, transfected or infected with a vector according to claim 34.
41. (Withdrawn) A method of identifying compounds capable of preventing or accelerating Gas1 mediated cell death comprising the steps of:
- (a) contacting a cell, tissue or organism expressing Gas1 or a functional equivalent, derivative or bioprecursor thereof capable of inducing apoptosis in a cell with said compound to be tested; and
 - (b) monitoring the effect of said compound on the state of said cell compared to a cell which has not been contacted with said compound.
42. (Withdrawn) A method according to claim 41 wherein said cell in step (a) comprises a host cell, tissue or organism transformed, transfected or infected with a vector comprising a nucleic acid molecule encoding a protein capable of inducing apoptosis in a cell comprising an amino acid sequence according to Sequence ID No. 4 or a nucleic acid molecule capable of hybridizing to Sequence ID No.1 under conditions of high stringency.
43. (Withdrawn) A compound identifiable as an inhibitor or an accelerator of cell death according to the method of claim 42.
44. (Withdrawn) A pharmaceutical composition comprising a compound according to claim 43, together with a pharmaceutically acceptable carrier, diluent or excipient therefor.
45. (Withdrawn) A pharmaceutical composition comprising any of a nucleic acid molecule encoding a protein according to Sequence ID No. 4 or a nucleic acid molecule capable of stringent hybridization thereto; an antisense molecule capable of hybridizing to a nucleic acid molecule encoding a protein according to Sequence ID No. 4 under conditions of high stringency; or a protein encoded by a nucleic acid molecule capable of hybridizing to

Sequence ID No. 1 under stringent hybridization conditions together with a pharmaceutically acceptable carrier, diluent or excipient therefor.

46-47. (Canceled).

48. (Withdrawn) The method of claim 22, wherein said neurological disorder is any of, Parkinson's disease, Alzheimer's disease, Huntington's disease, amyotrophic lateral sclerosis, a neurological condition caused by thrombosis or cerebral trauma.

49. (Withdrawn) The method of claim 22, where said cardiovascular disorder is a heart attack.

50. (Withdrawn) The method of claim 22, wherein said autoimmune disorder is multiple sclerosis.

51. (Withdrawn) The method of claim 22, wherein said neuroendocrine disorder is necrosis of the pituitary gland.

52. (Withdrawn) An antibody capable of binding to a protein comprising an amino acid sequence according to Sequence ID NO.2 or Sequence ID No. 4.

53. (Withdrawn) A pharmaceutical composition comprising an antibody according to claim 52 together with a pharmaceutically acceptable carrier, diluent or excipient therefor.

54. (Withdrawn) A method for decreasing the expression of a protein that is lethal to a cell, wherein the protein normally induces the expression or activation of either the Gas1 protein or a protein in the signal transduction pathway of which Gas1 is a component comprising the step of: contacting the cell with a therapeutically effective dose of a compound identified by

(a) providing a cell, tissue or organism comprising a nucleotide sequence encoding a Gas1 protein or a functional equivalent, derivative or bioprecursor thereof, which is capable

of inducing apoptosis in said cell, and ii) a further sequence encoding a protein which is otherwise lethal to said cell in itself or in response to a lethal stimulus in the presence of Gas1;

(b) inhibiting function and/or expression of said Gas1 protein or functional equivalent, derivative or bioprecursor thereof or a protein in the apoptotic pathway of which Gas1 is a component;

(c) expressing said sequence encoding said otherwise lethal protein;

(d) contacting said cell with a compound to be tested; and

monitoring the effect of said compound on said otherwise lethal protein compared to an identical cell which has not been contacted with said compound.